atherosclerotic cardiovascular disease (ASCVD), there is an entire section on nonstatins, including the following paragraph on page 2913 in Section 6.3.2 of the guideline.

Clinicians treating high-risk patients who have a less-than-anticipated response to statins, who are unable to tolerate a less-than-recommended intensity of a statin, or who are completely statin intolerant, may consider the addition of a nonstatin cholesterol-lowering therapy. High-risk individuals include those with ASCVD, those with LDL-C ≥190 mg/dl, and those with diabetes 40–75 years of age. In this situation, this guideline recommends clinicians preferentially prescribe drugs that have been shown in RCTs to provide ASCVD risk-reduction benefits that outweigh the potential for adverse effects and drug-drug interactions and consider patient preferences (2).

This not an inconsequential point. In recent randomized controlled trials (RCTs), niacin and ezetemibe, when added to intensive statin therapy, both lowered low-density lipoprotein cholesterol (LDL-C), but the addition of niacin did not result in improved outcomes and was associated with safety issues (3,4). This is contrasted with a recently reported RCT in a high-risk acute coronary syndrome population with 1 high-risk feature, where addition of ezetemibe to a moderate-intensity statin was shown to be both safe and incrementally effective (5).

Second, they incorrectly state what the guidelines say about follow-up therapy. Although the guidelines no longer endorse arbitrary LDL-C goals, we are uncertain how the authors could infer that the guidelines require little or no follow-up therapy.

Figure 5, entitled "Monitoring Therapeutic Response and Adherence," and associated text on pages 2912 to 2913 indicate that the guidelines endorse follow-up lipids, especially LDL-C. Follow-up lipids are needed to not only determine attainment of the therapeutic response to the appropriate intensity of statin, but also to monitor adherence to statin and lifestyle therapy.

Both of these errors are serious threats to the appropriate use of this evidence-based guideline. We respectfully request that Maddox et al. submit an erratum to the journal to correct these inaccurate statements regarding the 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol to reduce the risk of atherosclerotic cardiovascular risk in adults.

*Neil J. Stone, MD, MACP
C. Noel Bairey Merz, MD
Karol E. Watson, MD, PhD
Sidney C. Smith, Jr., MD

*Northwestern Medicine
676 North St. Clair; Suit 600 (Cardiology)
Chicago, Illinois 60611
E-mail: n-stone@northwestern.edu

http://dx.doi.org/10.1016/j.jacc.2014.12.072

Please note: Dr. Bairey-Merz is a consultant to Gilead (grant study section), Pfizer, and Amgen; and has received research grants from the National Heart, Lung, and Blood Institute (NHBLI), Gilead, and the Flight Attendants Medical Research Institute (FAMRI). Dr. Watson is a consultant with Merck and Daiichi Sankyo, and has received grants from NHLBI, NIDDK, BD2K consortium (all NIH). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Maddox TM, Borden WB, Tang F, et al. Implications of the 2013 ACC/AHA cholesterol guidelines for adults in contemporary cardiovascular practice: insights from the NCDR PINNACLE Registry. J Am Coll Cardiol 2014;64:2183–92.

2. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889–934.

3. The AIM-HIGH Investigators. Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy [erratum, N Engl J Med 2012;367:189]. N Engl J Med 2011;365:2255–67.

4. HPS-2 THRIVE Collaborative Group. HPS2-THRIVE randomized placebo-controlled trial in 25,673 high-risk patients of ER niacin/laropiprant: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. Eur Heart J 2013;34:1279–91.

5. Blazing MA, Giugliano RP, Cannon CP, et al. Evaluating cardiovascular event reduction with ezetimibe as an adjunct to simvastatin in 18,144 patients after acute coronary syndromes: final baseline characteristics of the IMPROVE-IT study population. Am Heart J 2014;168:205–12.e1.

REPLY: Getting Guidelines Correct

Their Evidence-Based Recommendations for Use of Nonstatins Added to Statins and the Need for Follow-Up Lipid Testing

We appreciate the comments made by Dr. Stone and colleagues regarding our paper discussing implications of the 2013 American College of Cardiology/American Heart Association cholesterol guidelines (1).

As Dr. Stone and colleagues correctly point out, the guidelines did not forbid nonstatin lipid-lowering therapies, but rather suggested that clinicians "may consider the addition of a nonstatin cholesterol-lowering therapy" (1). At the time of the guideline release and our paper publication, there were no randomized, controlled trials (RCTs) that had demonstrated cardiovascular (CV) event reduction benefit with nonstatin lipid-lowering medications. Thus, our statements indicating that these nonstatin

medications did not have a strong recommendation for CV event reduction and our consequent conclusions suggesting that the guidelines might lead to significant decreases in nonstatin use were consistent with both the most current evidence at the time and the guidelines (2).

We appreciate the added clarification provided by the guideline authors, and note that their stated preference for drugs proven to reduce CV events is especially germane in the wake of the recently released IMPROVE-IT (IMProved Reduction of Outcomes: Vytorin Efficacy International Trial) trial, which demonstrated CV event reduction with ezetimibe (3). This new information, available after the release of both the 2013 guidelines and our paper, will have implications for cholesterol management, and we are currently exploring those in a new analysis of PINNACLE (Practice Innovation and Clinical Excellence) data.

We also recognize that the guidelines recommended low-density lipoprotein cholesterol (LDL-C) testing to assess appropriateness of statin response and medication adherence. However, our paper did not suggest that no LDL-C testing should occur under the new guidelines, but rather that "the new guidelines did not recommend treatment to target LDL-C lipid levels, thus rendering *repeated* on-treatment testing unnecessary" (italics our own) (2). Under prior guidelines, repeated LDL-C testing to determine whether a particular LDL-C target was achieved took place with regularity, a phenomenon that we demonstrated in our analysis and almost certainly under-reported, given the frequency with which LDL-C levels are checked by primary care providers (who were not included in our analysis). Thus, our conclusion that "the cost and inconvenience of repeated LDL-C testing to titrate statin medication to specific LDL-C targets would be reduced" is consistent with the guidelines (2).

We appreciate the added clarification provided by the guideline authors, and feel that it helps further provide guidance to clinicians seeking to optimize cholesterol management, and its attendant effects on CV event reduction, for their patients.

*Thomas M. Maddox, MD, MSc
William J. Oetgen, MD, MBA
John S. Rumsfeld, MD, PhD
*VA Eastern Colorado Health Care System
Cardiology Section (111B)
1055 Clermont Street
Denver, Colorado 80220
E-mail: thomas.maddox@va.gov
http://dx.doi.org/10.1016/j.jacc.2015.02.057

Please note: Dr. Maddox is supported with a VA Health Services Research and Development career development award. Dr. Oetgen is the Executive Vice President for Science, Education, and Quality of the American College of Cardiology. Dr. Rumsfeld is the Chief Science Officer for the National Cardiovascular Data Registry.

REFERENCES

1. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889–934.

2. Maddox TM, Borden WB, Tang F, et al. Implications of the 2013 ACC/AHA cholesterol guidelines for adults in contemporary cardiovascular practice: insights from the NCDR PINNACLE registry. J Am Coll Cardiol 2014;64:2183–92.

3. Cannon C. IMProved Reduction of Outcomes: Vytorin Efficacy International Trial. 2014. http://www.eas-society.org/fileArchive/IMPROVE%20IT%20-%20PRESENTATION%202014-11-17.pdf. Accessed February 7, 2015.

Beta-Blocker Variability in Treatment of Long QT Syndrome

What Is the Confounder?

We read with great interest the observational study of patients with long QT syndrome (LQTS) by Abu-Zeitone et al. (1) published in a recent issue of the *Journal*. The key points noted by the authors include equal efficacy of 4 beta-blockers in the general LQTS population in reducing the risk of first cardiac event; however, in patients with LQT2, nadolol appeared to be the only one with significant risk reduction. In the high-risk patients with cardiac events while on beta-blocker therapy, propranolol was found to be the least effective (1). This study was conducted in the background of studies implicating propranolol as having a higher propensity to block wild-type hERG (human ether-a-go-go related gene) channel, which is involved in the pathogenesis of LQT2 (2); and differed from a recent study showing no difference in the efficacy of different beta-blockers in preventing cardiac events in a smaller sample of LQTS patients (3).

In the existing literature on beta-blockers spanning more than half a century, there has been no major study demonstrating a difference in efficacy of beta-blockers in heart rate reduction. Hence, we believe that measuring heart rate pre- and post-use of beta-blockers can be an effective surrogate marker of appropriate dosing and compliance. The authors do mention in their study limitations that registry database provides reasonably reliable information about patient compliance; however, no mention has been made about the heart rate response on the different